My name is Joon Lee, I am an interventional cardiologist and I am involved in the Transcatheter Aortic Valve program which is one of the things that I’ll be talking about and I’d like to give you an update on aortic stenosis. Obviously the disease has been with us forever, it’s changing in terms of how we think about it and certainly how we treat it. My disclosure is that I am one of the investigators in the Medtronic CoreValve Trial and that’s one of the devices that you’ll be seeing. I don’t receive any financial royalty. And probably my biggest disclosure is that I’m a relatively enthusiastic adopter of technology, so you’ll have to take what I say with that bias in mind.

Before I begin to get into the meat of the talk the part that I’m going to talk about in terms of our own efforts at transcatheter aortic valve therapy is really very much a team effort and it’s really the future in terms of how we go about treating complex disease and really delivering complex care, very much a multidisciplinary care and this is a partial list of the team that is required just to treat the patients. As you can see any of the physicians here or the ancillary staff could be giving this talk and I just happen to be the talking head for the day.

So what I’d like to do over the next 25 minutes or so is to talk a little bit about the natural history of aortic stenosis, review that, talk about the treatment of aortic stenosis and the gold standard which is a surgical aortic valve replacement, and then talk about transcatheter aortic valve implantation or replacement. They are used interchangeably so don’t get confused if you see two different names and I can give you a little story on why the name is changing in literature and lay press. And then if we have time a short case presentation which highlights some of the technology and some of the options that we have currently.
Well there are many different causes of aortic stenosis and those of you who have been in practice for a while will note that the etiology for aortic stenosis, the most common etiology is changing a little bit probably around the world and 40 years ago rheumatic valve disease was the most common. But mostly what we deal with now is senile calcific aortic stenosis and that’s what I’m going to focus on, this is the disease of the elderly and it’s the most common disease that we as cardiologists in the United States as well as primary care physicians will be seeing. The bicuspid valve you tend not to see the congenital bicuspid valve where the kids are born with a stenosed valve, what we see is the bicuspid valve which causes turbulence and which causes very similar pathology to the senile calcific aortic stenosis except the time course is shifted, so people with bicuspid valve will present in their 40s and 50s and 60s, whereas a tricuspid valve senile calcific stenosis usually presents in the 70s, 80s and 90s and even the centenarians.

So just to take a quick review of normal anatomy, this is a very nice Netter drawing where the aorta and the left ventricular outflow tract has been filleted. The normal aortic valve has 3 cusps, the semilunar cusp you will remember from medical school and the left coronary cusp, right coronary cusp. And this picture tells us a couple of things. This is what it should look like, it’s a real supple structure that moves very freely and it is very close to the mitral valve apparatus and that’s often lost in a lot of people who don’t deal with this pathology on a daily basis. This is a nice picture which shows this is the aortic valve which sits just behind the pulmonic valve and it sits actually anatomically very close to the mitral valve and the tricuspid valve. In the closed position this is what it’s supposed to look like, in the open position it opens up fully like that.
Well what happens in calcific aortic stenosis? I left the picture here because it makes us cardiologists feel like we know what pathophysiology really is, but the pathophysiology is best seen somewhat similar to the inflammatory and the degenerative process that occurs in atherosclerosis. So there is some involvement probably of hyperlipidemia and other inflammatory factors that are known to affect atherosclerosis but what happens is that very thin structure becomes – looks like this which is a surgical specimen from an aortic valve replacement. You get inflammation, you get thickening, you get calcium deposition and generally a stiffening of the tissue so that the valve no longer opens very well, present in the 60s, 70, 80, 90s as noted before.

Here is a picture of aortic stenosis in the operating room. This is actually bicuspid valve, you are looking straight down at the aorta which has been transected. You can see in contrast to the Netter drawing you can see all these calcium depositions, they are like little pebbles and it’s easy to imagine that this valve is not going to open up very well. Even though it’s bicuspid the tricuspid senile calcific aortic stenosis is very similar to this.

This is a rheumatic aortic stenosis which actually looks somewhat different, it’s also very thickened and there is fusing of the raphe or the opening, the commissures or whatever that separate the valve leaflets but you can see that there isn’t the same level of the pebblish type of deposition, so the pathophysiology is somewhat different even though the function is very similar.
This is what aortic – a normal aortic valve looks like in echo, this one will not run unfortunately but the rest of them hopefully will run. And this is in profile, this is the left ventricular outflow tract, this is the aorta so-called peristernal long axis but you see this very thin structure here, it’s almost like described as hands clasping in prayer position, that’s what a normal aortic valve should look like. And when you read an echocardiogram you will also get a Doppler report, if you order an echocardiogram. And what it will tell you is the velocity of the blood that’s going through the aortic valve just like your local state police can use their Doppler to see how fast you are going home on I-279 we can interrogate the LV outflow tract in the same manner. And a normal heart will eject the blood at about 1 meter per second. See cardiology is very simple, it’s a very simple number to remember, 1 meter per second is what a normal velocity through the LV outflow tract is.

This is another surgical specimen once again demonstrating what calcific aortic stenosis looks like. An echocardiogram, I’m going to show this echo later but basically what happens is that you’ll see in the same structure left ventricle aorta here that this is no longer a thin structure, a thick structure which does not move very freely. And like I said, remember I said that 1 meter per second is the normal velocity, what happens is just like when you were a kid when you put your finger on a hose you can create a jet of water coming out, as it narrows the blood velocity increases. If you look at this lady with aortic stenosis the velocity is no longer 1 meter per second but 5 meters per second. So that’s one of the ways we measure how much stenosis there is by measuring how fast the blood is flowing through the stenotic aortic valve.
This is what it looks like in the cath lab, this is basically a ventricular tracing, this yellow tracing is what a catheter in the LV looks like. During diastole the pressure is about 15 or 20, during systole it is 220 but the aortic pressure is only about 150 or 160. So this white area represents the gradient across that aortic valve. An LV systolic pressure obviously 220 may be okay if you are a giraffe and have to you know inject blood all the way to the head but it’s not a particularly healthy state to be in for the heart.

So what are the numbers that you want to remember? One of the take home messages and the numbers I’d like for you to remember if you can are these three. Severe aortic stenosis how do we measure it? Remember that velocity? The velocity over 4 meters per second is one of the definitions of severe aortic stenosis. The gradient, the same gradient I showed you, it can be measured in echocardiogram in the cath lab, a mean gradient of over 40 millimeters of mercury is also deemed severe aortic stenosis. The valve area that we get is always a calculated value, it’s not a direct measurement but a calculated measurement. But a valve area of less than 1 is deemed severe aortic stenosis. So you’ll see these three numbers shown again and again in multiple guidelines, velocity of 4, mean gradient of 40 and valve area of less than 1.

What are the symptoms of aortic stenosis? You really can’t get through internal medicine or medical school without some cardiologist asking you what are the three cardinal symptoms of aortic stenosis and no, they really haven’t changed over the last 50 years. The three cardinal symptoms are still angina, syncope and congestive heart failure. Why do these three things stick? Well I think that many of you will remember seeing this graph, this is a landmark paper from Braunwald in 1968 and
what it basically shows you is the survival by percentage and with time on this axis. And what happens is that if you have aortic stenosis at least in this era if you were relatively asymptomatic survival was quite good. It’s a very flat survival curve but once you develop symptoms then survival plummets. And this is where the teaching comes in, it’s not you are asymptomatic you are totally safe. Whether that’s true or not I’ll talk a little bit about some of the modifications we need to have on that thought but still the thought that angina, syncope and failure are the things that we want to always look for when we are following aortic stenosis patients still applies. You’ll see that this is a very old graph because see the age of the inflection point is in the 60s, so they are probably talking about a lot of people with rheumatic aortic stenosis and bicuspid aortic valve whereas if you made a graph like this today you are probably talking about inflection point about 75 or so because we are mostly dealing with senile calcific aortic stenosis.

Well what is wrong with the thought that we can just follow patients indefinitely? What happens to asymptomatic patients? This is from one of the echo labs, they followed 622 patients who came into the echo lab who were truly asymptomatic or deemed asymptomatic and met the criteria for severe aortic stenosis and they followed to see what happened to them. If you look at it within 3 years about 50% of them either developed symptoms or underwent aortic valve replacement or had another cardiac event. So just to say severe aortic stenosis if you are asymptomatic you should forget about it is not really the right message. The fact is they have a very high incidence of cardiac events and the question is how aggressive should we be in this population? The markers of poor outcome are advanced age, heavy calcifications and once again their velocity, the higher the velocity, higher the gradient worse the prognosis is.
So that’s how aortic stenosis develops and that’s how we detect it, mostly with echocardiogram, maybe in catheterization. How do we treat aortic stenosis? So medical treatment has been frustratingly ineffective; there is no effective treatment of aortic stenosis once it develops. Once again from the pathophysiology there was a lot of thought and the drug companies were incredibly optimistic that they had found another indication for statins. Unfortunately the large trials, large randomized trials have not been able to show any slowing down of progression of senile calcific aortic stenosis with aggressive statin therapy. That’s not to say there is no effect, but not enough to make a huge difference. Surgical treatment is the gold standard and we’ll go through that, we’ll talk about balloon valvuloplasty and then the transcatheter aortic valve implantation.

So this is kind of a, you know, around the world tour of the prosthetic aortic valves. You’ll see in C that is the Starr-Edwards, that was the first valves that were developed if you will, incredibly durable although the gradient profile was not that great but some have lasted 30 years. So the first aortic valve replacements were done in the ‘60s, so before that we really had no effective treatment with aortic stenosis, before that we simply watched the natural history of aortic stenosis. G and H are two that I’m going to talk about a little bit, those are the transcatheter aortic valves that are available.

The problem with surgical AVR is it works really well but it requires surgery and this is a picture, it requires that your heart be exposed, you go on the cardiopulmonary bypass machine, this is a valve that’s being sewed in. It will be inserted into this patient. But on the other hand, always remember that it works very well and it is still the gold standard for treatment of aortic stenosis.
So how good are our surgical colleagues? Well it turns out they do a great job. This is the STS, so this is the overall for isolated aortic valve replacement mortality in the United States. So overall mortality during this decade it hasn’t really changed, you are talking about 2 ½ to 3% which is pretty darn good for a surgical procedure that is as invasive as this. So if you are a low risk person, if you are 55, if you are 65, no comorbid conditions and you require it, you have severe aortic stenosis and you require AVR you should really expect a mortality of 1% or less in good hands and in good institutions. However the problem is the population that we are dealing with is getting older and they are sicker, and you can see here exactly what happens as patients get sicker. As your neuro-card association increases from 2%, I mean from 1 to 2 to 4 mortality more than triples. And as your age increases mortality will increase, comorbid conditions will increase mortality and that’s one of the problems that we are facing now.

So if you take everything that we just talked about, remember this curve, what happens to you with aortic stenosis, right, there is an inflection point once you develop symptoms with severe aortic stenosis and surgery like I said is pretty darn good in terms of making patients better. In fact so good the thought and the teaching points are that if you have surgery and are able to survive it that your life expectancy mirrors someone else that same age without aortic stenosis; so the concept is if you can just get people through so that you replace their valve then they get back to the regular curve in terms of mortality and hence this recommendation surgical intervention should be performed once symptoms occur.
So with that evidence in mind then it’s kind of easy to understand why we have the guidelines we do. So this is basically a schematic drawing of the ACC and American Heart Association Guidelines for treating aortic stenosis. Remember those numbers I talked to you about, severe aortic stenosis defined by velocity greater than 4 meters per second, aortic valve area of less than 1 sq. cm, mean gradient over 40. I’m going to go through this but you’ll see what the take home message is. So if you have that and you need some type of cardiac surgery sure, you should get that replaced because while they are in there they should fix it. If you have symptoms you should get your valve replaced, you end up down here. If you don’t have symptoms or it’s not so clear this is a big question. So if you have an 85 year old patient and you ask them are you have any symptoms of aortic stenosis and limit it, that’s probably not that adequate. You know if they have significantly modified their lifestyle because of aortic stenosis that doesn’t mean that they are not having symptoms, that just means they’ve modified their lifestyle so that they don’t necessarily feel it every day. So although many people are taught that you should never do exercise testing in aortic stenosis that’s really not the current thought. If you are worried about it it’s better to put them on a treadmill, let’s see what they do because you can then see if they are really limited or not and should undergo aortic valve replacement.

So in order to escape aortic valve replacement according to these recommendations you have to be totally asymptomatic, have normal LV systolic function and have these low risk factors. Then you go down this pathway. Then the recommendation is every 6 months or 12 months to repeat the whole process. So the take home message is that if you have severe aortic stenosis and the patients are well enough to be treated it’s likely that they are going to get treated relatively soon and the
threshold should be relatively low for treating it because it’s not like they can go 10 years without it, the rate of progression is such that if you have for example a relatively healthy 72 year old patient whose got severe aortic stenosis you know threshold should be pretty low for treating it given the success of the modern treatment.

If you take that then it’s very surprising that we get data like this. This is a survey of United States and European Union, so relatively advanced countries. And these surveys suggest that despite the relatively high prevalence of aortic stenosis in the elderly population that somewhere between 30 to 60% of the patients who have identifiable symptoms are not undergoing surgical AVR. Why is that the case? I think part of it is our perception of how invasive and how, if you will, dangerous aortic valve replacement is, and also potentially a misperception about survival rates.

I always like to look at this, that is you know we always tend to think our patients tend to think look 78 or 80 is the mean age of the population but the fact is if you hit age 75 your expected lifespan is over 11 years in this country. In fact if you are 85 your expected lifespan is over 6 ½ years. So in terms of treating a disease that strikes mainly the elderly like aortic stenosis you have to keep that in mind and once again make decisions based on those expected life expectancies not because you’ve already outlived what is a mean life expectancy.

And how do elderly do with surgical aortic valve replacement? Not that bad, not perfect though. So if you look at, this is a Euroscore, like STS it identifies what the surgical risk is and their numbers they are not exactly perfect but in the low risk population of octogenarians basically, red being 30
day survival, yellow being 1 year survival. 1 year survival after aortic valve replacement was 90%, which is pretty good. And you’ll see how bad survival is in the natural history of aortic stenosis. Obviously as the risk increases 1 year survival goes to 78, 69%, still not bad but pretty high risk.

That covers surgery, how about balloon valvuloplasty? You know as an interventional cardiologist obviously when you see a narrowing it’s incredibly attractive to try to blow that up, which is basically what we do. This is a cartoon of how the balloon goes across it and how the balloon valvuloplasty is performed, and this is basically a picture of the, an actual valvuloplasty. There is a catheter from the aorta to the LV, and those are manually blown up. And you saw that as it was going up there was a little bit of what we call a waist, that’s where the narrowing was and balloon literally just stretches that valve that you just saw. So this was greeted with tremendous enthusiasm in the 1980s because it seemed to work. This is a pressure tracing again, the gradient that was like this would immediately go down to half and it seems like a great thing and patient tolerated okay at that point. The problem is that it’s not particularly effective in terms of changing the natural history. This is the survival following balloon valvuloplasty, it recurs in about 50% of the patients within 6 months and there was a 100% absence of mortality benefit, people died at the same rate. It is a good palliative procedure for the right people, but does not have any significant sustained benefit. So we only use it occasionally as preparation for transcatheter valve I’ll show you. If you come in shock and have severe AS it may be useful and one of the other places is people will sometimes come with underdiagnosed aortic stenosis breaking their hip requiring surgery in which case we may do the valvuloplasty to tide them over to surgery.
So the big revelation over the last 10 years is the transcatheter aortic valve implantation. So in 2002 about 40 years after the first surgical aortic valve replacement the transcatheter aortic valve replacement was approached. So this is the Edwards SAPIEN valve which is the FDA approved transcatheter aortic valve, the first one done in France was somewhat of an early form and modification of it. It requires a very large delivery system, it is made of bovine pericardial tissue with a metal around it that can be if you will folded into a catheter. I’ll just show a quick picture here, this is the catheter going up. The only reason I show it is, hopefully you can see it from the back, there is a thin catheter here beside it. That’s the catheter we’ll usually use for diagnostic procedures, it’s about 1.8 mm in diameter. This is the catheter size of the transcatheter aortic valve, even though it’s done through a catheter it is not the same procedure. This is about 7 or 8 times larger in diameter than the catheter that we use for diagnostic procedures. We do a valvuloplasty to prep the valve before and this is a picture of how the procedure is done. And this is the valve that’s folded. This metallic structure is the same valve I showed you in the cartoon that is loaded onto a catheter that is now being pushed across the aortic valve, so the whole thing is done with the operator sitting much like the catheterization outside of the body pushing the catheter and manipulating it with x-ray guidance.

And this is the sequence of actual valve implantation. You can see we make the heart go really fast, we pace it because ideally what we really like is asystole and cardiac standstill but that tends not to be compatible with life so we can’t really do that. So we simulate it by pacing the heart at a rate of about 200, that decreases the cardiac output and then you saw the balloon go up and the valve is now inflated and stops there. So this procedure is like playing a hockey goalie, that is it takes a lot of tie
to prep it and then there is about 15 seconds which is basically the sequence as recorded here. You pace it and then you see someone is pulling this pigtail catheter back and then we have to make a decision that is placed in the right place. And then as it goes up sometimes it will move; if it moves and if it’s too high that’s not compatible with life, if it’s too low then it will not function. So it’s one of those procedures where after 15 second either everything looks really good or things look really bad. But fortunately things tend to – with skilled hands things tend to work very, very well.

So this is what the cartoon looks like, this is where the valve sits. So what’s happening is that we are actually pushing the old valve just totally to the side, a new valve just folds out in its place. And this is the SAPIEN Edwards valve which is FDA approved which sits in the fashion as shown in this cartoon, the coronary ostium are above it.

This is the Medtronic CoreValve which is not FDA approved but the second most popular valve in the world. It’s somewhat different in that you can see that the metal cage is larger, instead of bovine it’s porcine pericardial tissue, it is a slightly smaller delivery system and it’s made of an interesting metal called nitinol which retains its shape. So instead of using a balloon to stretch it out it comes in this shape and as you’ll see we put a sleeve to fold it and then it just folds out or flowers by itself. And the real reward is if everything goes well this is an actual patient that came and visited us on Tuesday, one week after transcatheter aortic valve implantation. And that’s the entirety of his scar. This was proceeded through a subclavian access so much like where the pacemaker would be but that’s all the scar that they have, not the median sternotomy and the others that are required for surgical AVR.
These are the two valves that are popular to use, FDA approved, this will likely be FDA approved in a year. As you might imagine this is big business so there are hundreds of valves that are being developed, only few of which will ever make it to market but these are all the designs that are currently being tested mostly in Europe.

So I’ll spend a few minutes talking about the PARTNER Trial because it is the trial which changed the landscape for us in the field. The PARTNER Trial was the landmark trial which tested the SAPIEN valve and actually led to FDA approval. Severe AS very similar criteria, only thing different remember is that the aortic valve area instead of 1 sq cm became 0.8 sq cm, you had to have symptoms and patients had to be of high surgical risk, meaning expected mortality of greater than 10 or 15%. And the design was simple and elegant if you will, inoperable patients were randomized to either medical therapy which is basically regular therapy, or to transcatheter aortic valve. I would ignore the two access points for now. High risk patients were randomized to surgical aortic valve replacement versus transcatheter valves.

And the results many of you have probably seen, I hope you can see the yellow. In the inoperable patients after 1 year the mortality in the yellow in the standard care treatment was 50%. The mortality in the transcatheter aortic valve implantation was 30%. There are two things that are incredibly impressive about this. One is how lethal severe aortic stenosis is. I doubt you could show me many cancer trials where a 1 year mortality is 50%, it’s basically like stage IV cancer. And even though the improvement and absolute difference of 20% mortality is an incredible improvement
even the transcatheter aortic valve replacement patients died at a rate of 30% by year 1 and it continues to increase in year 2. The other thing to note, this is the same group, is not only is the death curve continuing to if you will separate and it’s now out to 3 years, rehospitalization is significantly higher in the standard therapy group compared to the transcatheter aortic valve replacement. So it’s not like these patients just simply die, it’s that they get sicker and sicker as time goes on as the disease progresses.

So-called the high risk cohort where the patients who were deemed to be surgical candidates but significantly elevated risk calculated risk of about 10% mortality and after one year in this population they are basically deemed to be non-inferior equivalent therapy, the death rate is about 24 or 25%. And you can see the two curves basically depending on how you put the end points overlap each other. This is the stroke, that’s one of the controversial areas in our field, so I would say that the bottom line right now is that the transcatheter therapy definitely do not decrease stroke rate in terms of aortic valve replacement, whether it’s higher than surgical AVR or not is somewhat controversial, most of us think that it’s about equivalent to the surgical AVR but still remains somewhat untested.

I’m going to say a couple of things about how this was FDA approved. That trial led to FDA approval of transcatheter aortic valves and it’s really informative because unlike every other technology in May of 2012 there was a statement, a CMS national coverage decision but it’s unique, I’ve never seen coverage decision like this. It specifies that off label use will not be paid for. The reason I point that out is coronary stents which go in at a rate of about a million a year in the United
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States we know that in the United States about 50% of coronary stents are actually used for off label use. And nobody asked the insurance companies don’t ask whether it’s off label or not, they are still paid for. In this technology it specify a priority that off label use will not be paid for. It also specifies that an interventional cardiologist and a cardiac surgeon has to be present and scrubbed and together for the procedure. No other coverage decision that I know of says that what type of person must be there during the procedure, it does specify what the minimal requirement for the hospital and the surgeon and the interventionalist is here. So it really ushers in a new era of teamwork. This is kind of the typical you know a surgeon, cardiac surgeon, I don’t know which one is the cardiac surgeon and which one is the interventionalist but that’s usually what we typically think of teamwork there. In a procedure like the transcatheter aortic valve it really requires teamwork for the centers that do it well.

This is the hybrid OR where we do the procedure. You know that is where you will recognize this isn’t a cath lab because we tend not to practice such sterile technique but it’s definitely though where everyone is wearing hats, masks and basically if you look at it you know here is a cardiac surgeon, an interventional cardiologist actually working together and manipulating the catheter together, actually making the decisions together intra-procedure in terms of when to deploy the valve.

Just a couple of things about our own program and a little plug for our program, we’ve been involved since January of 2011 at Presby-Shadyside, the team I showed you in the beginning, and this is the results through June 30 of 2013. We have to date done over 155 implants, as you can see it’s kind of doubling every year because how the field is going. There are in the United States about
250 implant centers across the country, most are doing 20 to 25, we are at the rate of doing probably about 100 a year. We’ve done more CoreValves than SAPIEN because we’ve been involved in the trials. Basically the age population, this is typical of the trials that have been done, our average age is 84, our oldest is 95 and youngest is 57. STS score which predicts mortality, the predicted mortality on average of our patients was greater than 10%. You can either go in through the leg, subclavian or you can puncture the aorta directly or through a thoracotomy so-called direct, a transapical approach. Our morality for 30 days we’ve lost unfortunately 5 patients which gives us a 5 – 30 day mortality rate around 4%. We do have a stroke rate which is about expected at most large centers, a little bit less than 3%. We’ve been fortunate to have a very low vascular complication rate but it does happen.

We are proud of our results, the 30 day death rate is 4%. Most centers, PARTNERS as well as the largest registry in Europe are currently reporting about a 10% 30 day death rate with transcatheter aortic valve. You know our follow-up is somewhat limited because we’ve been doing it for about 2.75 years, we have an 11% death rate at one year which is much better than what we would expect. Still not perfect, once again this is an incredibly morbid and high risk disease with a lot of mortality, obviously this offers a lot of different options for the patients.

I would like for you to remember that basically symptomatic patients with severe AS have really poor outcomes and that’s proven again and again and that’s not any different in 2013 as it was in 1968. Surgical AVR really is the gold standard and a very good gold standard for most patients. There is a significant problem with the perception of the surgical AVR in the elderly is much more
dangerous that I believe it really is, even the elderly, somewhat frail patients can derive a lot of benefit and we should be considering that and I think there is an overall undertreatment of aortic stenosis. Compared to medical therapy in end stage patients transcatheter aortic valve implantation seems to offer a lot of hope. We have one FDA approved valve, another valve that’s on the way and the field will continue to develop. We don’t know how long these valves are going to last, we do know at the 3 to 5 year range there seems to be no deterioration. Surgical valves I would tell you will give you a mean expectancy to 12 to 15 years, is it going to last that long we just don’t have answers to that because they haven’t been around that long.

So the current status is remember the 3 numbers, if a patient is a nonsurgical candidate they should be considered for transcatheter aortic valve implantation. If they are high risk for surgery they probably should be considered for transcatheter aortic valve implantation. If they are intermediate risk, predicted risk of 4 to 9% mortality from surgical AVR we don’t know what to do with them, we are actually activating and enrolling patients like that in a randomized trial between surgical aortic valve replacement and transcatheter aortic valve replacement.

So I apologize for running late and I’ll be around here if someone has individual questions later. Okay.